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Translating silicon nanowire BioFET sensor-technology to embedded point-of-care medical diagnostics

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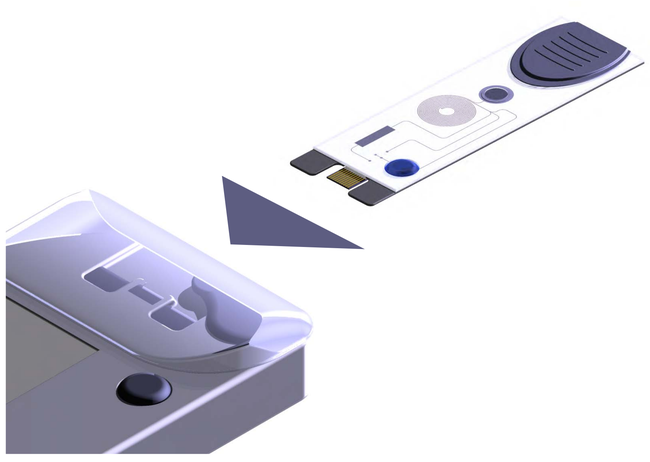
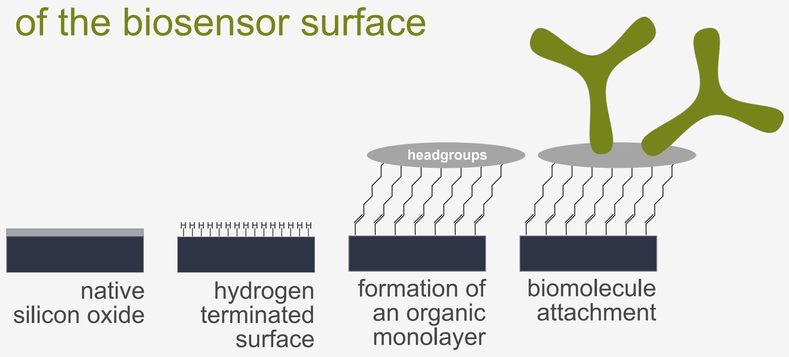


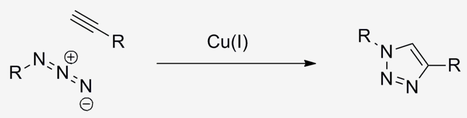
Many modern diagnostic tests require the fast and accurate determination of the presence of certain proteins (biomarkers) in blood or other patient samples. Depending on the expected diagnosis a specific set of different biomarkers is usally needed in order to make a reliable decision on how to proceed in terms of further tests or therapy. For this purpose, we are developing a highly flexible biosensing platform using silicon nanoribbons in a field effect transistor configuration. Different aspects of the translation of the biosensor into an autonomous point-of-care device are being addessed.

functionalization
of the biosensor surface



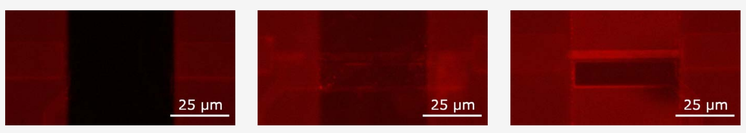
silicon surface modification A

The images show functionalization layers of 1,7-Octadiyne labeled with a Fluorophore-Azide using a copper catalyzed Azide-Alkyne cycloaddition CuAAC



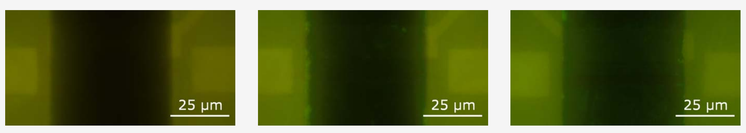
on a) **silicon surfaces** (scratched to present different cystal surface orientations)

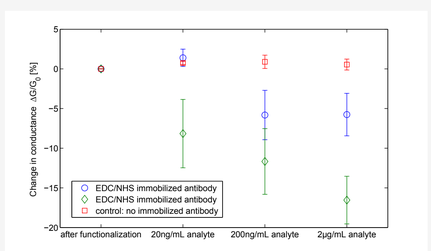
and b) **polysilicon nanoribbons**



silicon surface modification B

The images show the result of the binding of a fluorescently labeled goat anti-mouse antibody to an immobilized mouse-antibody. The surface has been modified with an alkyne presenting a BOC protected amino group. An the antibody was then immobilized by EDC/NHS aminocoupling after removal of the BOC group.

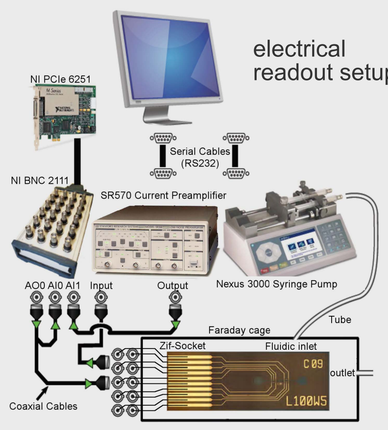


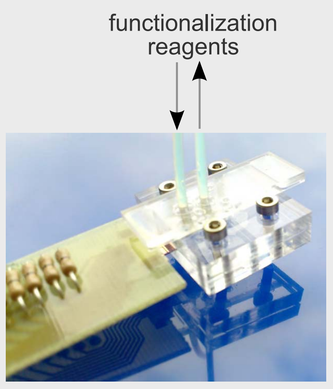


antibody detection

The graph shows the detection signal as the differential conductance measured for different concentrations of the second antibody as analyte..

sensor integration
and microfluidics

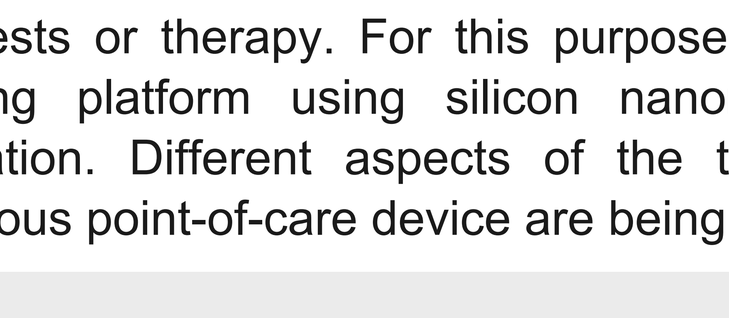




simple flowcell to interface the sensor chip

monitoring surface preparation

The graphs show the recorded current through the nanoribbon during oxide removal and polysilicon etching in aqueous 1% HF solution for different etching times.



etching starts at the injection of HF and continues during the time in air, probably due to HF remaining on the surface and in the material

longer etching phase leads to complete loss of conduction due to decomposition of poly-silicon in the nanoribbons

simultaneous reagent delivery to 4 sensors in two flow paths

flowcell with reagent mixing driven by gravity

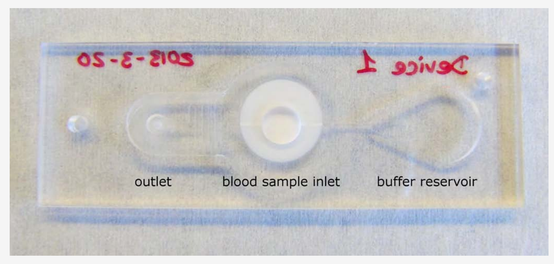
conclusions

two functionalization schemes have been demonstated for the direct attachment of proteins to a poly-silicon nanoribbon surface.

surface modification and analyte attachement can be **monitored electrically.**

devices for **plasma extraction** from small blood samples are being investigated

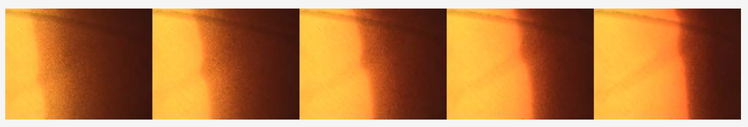
sample handling
from a finger prick



plasma extraction filter

The image shows a simple device employing a membrane filter to remove cells from a small blood sample to extract the plasma and realese it into a stream of buffer. In this way the buffer can be adjusted to increase sensitivity.

The microscope images show the receding meniscus of the blood sample, as the plasma is removed and the only the cells remain.



outlook

biomarker detection - NKG2D (immun cell receptor) ligands and hypoxia marker CA9 are under investigation as potential cancer markers. Sensor functionalization with these proteins is currently tested.

passive flow control and self-terminating functionalization by capillary/gravitational forces

improved sensor design to enable **multiplexing** using several flow paths

optimization of the functionalization protocol for **improved sensitivity**

undiluted plasma extraction using a receptor pad and **capillary networks**

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